REMARKS

STATUS OF THE CLAIMS

Claims 1-124 were pending and claims 1-26 and 66-71 were examined.

By amendment herein, claims 1-65 and 72-124 have been canceled, without prejudice or disclaimer. Claim 66 has been amended as shown above to recite a clone that is a member of a library obtained according to specific process steps, as described for example in original claim 13; on page 28, lines 1-5; page 30, lines 20-26; page 36, lines 15-20; page 51, line 16 through page 52, line 2 and page 31, lines 6-12 (step (c)). New claims 125-128 have been added and find support, for example, on page 36, lines 21-24 (claims 125 and 126); page 54, line 16 through page 55, line 4 (claim 127); and page 28, lines 1-5; page 36, lines 15-20; page 51, lines 21-23 (claim 128). Claims 67-71 have been amended to properly depend from claim 66 and are directed to libraries made of a plurality of sequences according to claim 66.

Claim 66, as amended, recites embodiments covered by original claims 2, 3 and 13 and therefore comports with the Restriction Requirement presently in effect.

Thus, claims 66-71 and 125-128 are pending as shown above.

REQUEST TO CHANGE INVENTORSHIP PURSUANT TO 37 C.F.R. § 1.48(B)

This Request is filed in order to correct the inventorship of the above-identified patent application under 37 CFR §1.48(b) so as to eliminate the inventors who did not contribute to the currently pending claims.

The inventors of the currently pending claims are **Alan WOLFFE** and **Fyodor URNOV**. The following individuals, originally named as inventors, did not contribute to the subject matter of the pending claims:

Dmitry GUSCHIN, Trevor COLLINGWOOD, Xiao-Yong LI, and Brian JOHNSTONE.

Thus, it is appropriate to remove these individuals' names from the list of joint inventors on the application. A check to cover the $130 fee is attached. Such action is respectfully solicited by way of this paper.

RESTRICTION REQUIREMENT

Applicants note with appreciation withdrawal of the Restriction Requirement as between Groups I, II, IX and X. For the reasons of record, Applicants reiterate that because Groups I through VIII share the same classification and subclassification, it would not be burdensome (and indeed save time and effort) for these Groups to be searched together. In any event, cancellation of claims 1-65 and 72-124 renders the Restriction Requirement moot. Applicants

expressly reserve their right under 35 USC §121 to file one or more divisional applications directed to any nonelected subject matter during the pendency of this application.

DECLARATION

As requested in paragraph 2 of the Office Action, Applicants submit herewith a revised declaration including the name, address and citizenship of Alan Wolffe's legal representative Elizabeth Wolffe.

INFORMATION DISCLOSURE STATEMENT

Applicants note with appreciation return of the signed and initialed 1449 forms indicating that all references except non-English language BK-1, DE19853398C1 and WO 00/31294 have been considered. (Office Action, paragraph 2).

Applicants understand that only the references submitted in an IDS will be considered by the Examiner. (Office Action, paragraph 3)

SPECIFICATION

A. Title

As requested by the Examiner in paragraph 6 of the Office Action, the title has been amended as shown above in order to be more clearly indicative of the subject matter to which the claims are directed.

B. Abstract

As requested by the Examiner in paragraph 7 of the Office Action, submitted herewith is a revised Abstract (on a separate numbered sheet).

C. Trademarks

In response to paragraph 8 of the Office Action, Applicants have capitalized and denoted the trademarked term "GENBANK™" wherever it occurs in the specification.

D. Embedded Hyperlinks

In response to paragraph 9 of the Office Action, Applicants have amended the specification to remove embedded hyperlinks, thereby obviating this objection.

35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 66-71 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not described by the specification as filed. (Office Action, paragraph 12). The Examiner makes several arguments in support of this rejection, including defining the claim term "library" based on an on-line dictionary. Furthermore, although the Examiner acknowledges that there is general knowledge and high level of skill in the art, it is nevertheless asserted that "the specification does not describe the structure (i.e. sequences of each clone of a library) of any species... ." On this basis, the Examiner concludes that one of skill in the art would not have concluded that Applicants were in possession of the claimed subject matter at the time of filing.

Applicants traverse the rejection and supporting remarks.

As a threshold matter, Applicants notes that the definition of the term "library" provided by the Examiner (based on Biotech Life Science Dictionary) comports with the definition set forth throughout the specification, for example on page 47, lines 28-29, which states that a library refers a population of DNA fragments that have been propagated in some type of a cloning vector. Applicants further note that the use of DNA fragments in the plural, throughout the application, indicates that the there are more than two fragments and, in addition, that these fragments are different.

Turning now to the rejection *per se*, Applicants remind the Examiner that fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117, emphasis added. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of the claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsis verba.* Rather, all that is required is that the specification reasonably convey possession of the invention. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981).

Furthermore, the Patent Office's own guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> [t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely **no** requirement that Applicants exemplify (or reduce to practice) all polynucleotide sequences falling within the scope of the claims in order to adequately describe the claimed libraries.

In the pending case, and contrary to the Office's assertion, the specification does contain representative examples of possible library clones, namely SEQ ID NOs: 10, 11 and 12. In any event, the adequacy of a specification's description is not judged by the number of examples, but by whether the specification, when read by the skilled artisan in light of the state of the art, contains sufficient disclosure regarding the claimed libraries to apprise one of skill in the art that Applicants were in possession of said libraries. It is axiomatic that the specification need only describe in detail that which is new or not conventional. (See, Guidelines on Written Description). In the case at hand, a skilled artisan reading the specification would have known that Applicants were in possession of claimed libraries obtained as set forth in the claims in view of the specification's extensive disclosure of (1) exemplary sequences falling within the scope of the claims; (2) extensive disclosure of the recited process steps; and (3) conventional, known methods of cloning polynucleotides to prepare libraries.

Furthermore, the Office's reliance of *Regents of the Univ. Calif. v. Eli Lilly* is misplaced. The written description requirement of § 112 is highly fact dependent and the claims, disclosure and state of the art in *Eli Lilly* are entirely different from those in the case at hand. Indeed, the issue in *Eli Lilly* was not whether those specifications disclosed a sufficient number of representative examples, but whether those specifications disclosed any structure at all. In fact, the application in that case was completely devoid of any representative structural (sequence) examples. Consequently, the Federal Circuit's holding *Eli Lilly* in no way necessitate that the claims be limited in scope to particular sequences.

Moreover, the Federal Circuit has recently confirmed that the test for possession of an invention does not require explicit disclosure of nucleotide sequence information. See, for example, *Moba B.V. v. Diamond Automation Inc.*, 66 USPQ2d 1429, 1439 (Fed. Cir. 2003):

> The possession test requires assessment from the viewpoint of one of skill in the art. [citing *Vas-Cath*] at 1563-64 ("the applicant must ... convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*") (emphasis in original); *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) ("The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed' ") (citation omitted). In Enzo and Amgen, the record showed that the specification that taught one of skill in the art to make and use an invention also convinced that artisan that the inventor possessed the invention. Similarly in this case, the Lilly disclosure rule does not require a particular form of disclosure because one of skill in the art could determine from the specification that the inventor possessed the invention at the time of filing.

Indeed, Judge Rader's concurrence in *Moba* warns that the Lilly decision is not only fact-dependent, but results in an unduly burdensome description requirement (*see, Moba B.V. v. Diamond Automation Inc.*, 66 USPQ2d at 1449):

> For biotechnological inventions, Lilly purports to require the recitation, nucleotide by nucleotide, of the entire sequence of a new protein [*sic*] or composition. . . . This burdensome disclosure standard is tantamount to requiring disclosure, for a new software invention, of the entire source code, symbol by symbol, including all source code permutations that would not alter the function of the software. Ironically, the Federal Circuit has expressly rejected such a requirement for software inventions, but apparently enforces the requirement for biotechnology. See e.g. N. Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 15 USPQ2d 1321 (Fed. Cir. 1990) (overturning a finding that a patent did not adequately disclose "batching" software). This discrepancy emphasizes another problematic aspect of the Lilly doctrine. That is, it imposes a different disclosure standard for biotechnology than for computer technology. Despite the technology-neutral language of the Patent Act, the Lilly rule imposes technology-specific requirements.

In view of the disclosure of the specification and the state of the art, it would have been plain to the skilled artisan that Applicants were in possession of the polynucleotides and libraries as set forth in pending claims 66-71 and 125-128. Accordingly, and consonant with statute and

with established case law, the rejection is improper. Consequently, withdrawal of this rejection is in order.

35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT

Claims 1-6 and 8-26 were rejected as allegedly not enabled by the specification as filed. (Office Action, paragraphs 13 and 14).

The foregoing amendments, which canceled claims 1-6 and 8-26 without prejudice or disclaimer, obviate these rejections.

35 U.S.C. § 112, SECOND PARAGRAPH

Claims 66-71 were rejected as allegedly indefinite. (Office Action, paragraph 16). In particular, it was alleged that the metes and bounds of the claims were not clear because the process limitations of claim 3 were not set forth.

As noted above, claim 66 has been amended to positively recite process limitations. Thus, the metes and bounds of the claims would be clear to the skilled artisan and withdrawal of this rejection is in order.

35 U.S.C. § 102(B)

Claims 66-71 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Clontech Catalogue. (Office Action, paragraph 17). In support of this rejection, the Examiner asserts that the use of the term "comprising" must be interpreted to read on libraries that include sequences that correspond to inaccessible regions. It is noted that process limitations do not, in and of themselves, impart patentability. Accordingly, the Clontech Catalogue is alleged to discloses multiple genomic libraries made from different organisms with cellular chromatin.

As a threshold matter, Applicants note that the Office's statement "These genomic libraries are made by a method involving digesting the whole genomes of the chromatin of different organisms with Sau3A I or Mbo I . . . and cloning the resulted [*sic*] fragments in different vector systems." is unclear. In particular, the meaning of "the whole genomes of the chromatin of different organisms" is not clear.

In any event, Applicants point out that the genomic libraries disclosed in the Clontech Catalogue were obtained by digesting naked genomic DNA. By contrast, the pending claims require that the claimed polynucleotides and libraries be obtained by digestion of cellular chromatin (not naked DNA). This process limitation imparts a unique property to the claimed polynucleotides and libraries: namely that the inserts in said libraries consist essentially of sequences from accessible regions of cellular chromatin. Since the libraries disclosed in the

Clontech Catalogue comprise polynucleotides that do not correspond to accessible regions (as acknowledged in the Office Action at page 12, lines 2-7), they do not consist essentially of accessible sequences, and therefore cannot anticipate the presently claimed subject matter.

Thus, the claimed polynucleotides and libraries are distinct from Clontech's libraries, not only by the process steps involved in making the libraries but also because, unlike Clontech's, the disclosed libraries consist essentially of insert sequences corresponding to accessible regions of cellular chromatin. Accordingly, the rejection cannot be sustained and Applicants respectfully request withdrawal thereof.

35 U.S.C. § 103

Claims 1-2, 4-9, 13-19, and 21-25 were rejected under 35 U.S.C. § 103 as allegedly obvious over van Steensel in view of Bringmann. (Office Action, paragraph 22). Claim 3 was rejected as allegedly obvious over van Steensel in view of Bringmann and in further view of Grosveld. (Office Action, paragraph 23). Claims 12, 20, and 26 were rejected as allegedly obvious over van Steensel in view of Bringmann and in further view of Gross. (Office Action, paragraph 24). In addition, claims 1-4, 10-11, and 13-15 were rejected as allegedly obvious over Grosveld in view of Tanguay. (Office Action, paragraph 25). Finally, claim 12 was rejected as allegedly obvious over Grosveld in view of Tanguay, further in view of Gross. (Office Action, paragraph 26).

The foregoing amendments, which canceled these claims without prejudice or disclaimer, obviate all of these rejections.

PROVISIONAL DOUBLE PATENTING

Claims 1-26 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over various claims in copending application no. 09/844,501 (the parent of the pending application). (Office Action, paragraphs 28 and 29).

The foregoing amendments, which canceled claims 1-26 without prejudice or disclaimer, obviate both provisional double patenting rejections.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

Respectfully submitted,

Date: December 8, 2004

By: _____

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